Notice of Allowability	Application No.	Applicant(s)	
	09/849,499	WALDMANN ET AL.	
	Examiner	Art Unit	
	Thaian N. Ton	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *11/15/06*.

2. ☒ The allowed claim(s) is/are *64,69,71,72,74,75,77,78,80-84,86-90,111,113-115,117,119-133*.

3. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☒ All b) ☐ Some* c) ☐ None of the:
      1. ☒ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date *2/2/07*.
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

PROPOSED EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Carol Francis on February 2, 2007.

The application has been amended as follows:

In the claims:

1. Replace claim 64 with the following:

64. A process for producing a culture of human dendritic cells, comprising: culturing embryoid bodies made from human embryonic stem cells, said culturing being in the presence of a composition comprising IL-3; and recovering human dendritic cells from said culture.

2. Cancel claim 70.

3. In claim 89, line 2, replace the term "ares" in with – are –.

4. In claim 90, line 1, replace the term "claim 112" with – claim 64 –.

5. Cancel claim 110.

6. In claim 111, line 2, replace the term "dendritc" with – dendritic –.

7. Cancel claim 112.

8. Replace claim 115 with the following:

115. A process for producing a culture of mouse dendritic cells, comprising: culturing embryoid bodies made from mouse embryonic stem cells, said culturing being in the presence of a composition comprising IL-3; and recovering mouse dendritic cells from said culture.

9. Cancel claim 116.

10. Cancel claim 118.

11. Replace claim 132 with the following:

132. The process of claim 115, wherein the mouse embryonic stem cells are from a CBA/Ca or a C57Bl/6 cell line.

12. Cancel claim 134-138.

In the specification:

1. Delete the text on page 6, line 25, beginning with "In the attached figures:" to page 7 line 2, ending with "the parent ES cell line."

2. Insert on page 6, line 25 the following:

Figure 1: Phase-contrast micrographs of ES cell-derived dendritic cells. (a) Low power view of an embryoid body 24 hr after plating onto tissue culture plastic, showing the emigration of stomal cells in a radial fashion. (b-c) esDC developing around the periphery of a colony. Note

the sharp demarcation between stromal cells supporting their development and those that fail to do so. (d) Appearance of clusters of esDC (arrows) similar to those apparent in cultures of mouse bone marrow. (e) esDC that have seeded areas of the dish uncolonized by stromal cells. (f) Cultures of putative lymphoid esDC maintained in IL-3 alone.

Figure 2: Electron micrographs of esDC cultured in GM-CSF and IL-3 showing typical DC morphology (a) and a propensity to phagocytose apoptotic cells (arrow), consistent with their immature phenotype. The bar represents 5μm.

Figure 3: Surface phenotype of esDC grown is GM-CSF and IL-3 assessed by flow cytometry. Filled histograms indicate levels of expression of CD44 (a), B7-1 (b), ICAM-1 (c) B7-2 (d), CD40 (e), CD11c (f) and class II MHC (g). Open histograms represent levels of background staining determined using irrelevant species- and isotype-matched control antibodies.

Figure 4: Immunostimulatory activity of esDC in the allogeneic MLR. esDC from the CBA/Ca ES cell line ESF116 were co-cultured with purified T cells from C57Bl/10 mice and the extent of proliferation was measured as a function of ^{3}H-TdR uptake 5 days later.

Figure 5: (a) IL-2 secretion by the T cell hybridoma, 2G7.1, in response to HEL presented by live esDC (closed symbols) but not DC that had been fixed first in paraformaldehyde to prevent antigen uptake (open symbols). (b) Stimulation of the 2G7.1 hybridoma is

inhibited by the addition of a mAb specific for class II MHC (closed symbols) but not by the addition of an irrelevant species and isotype-matched control antibody (open symbols).

Figure 6: Flow cytometric analysis of esDC following maturation induced by the addition of LPS to cultures. Filled histograms indicated the levels of expression of class I1 MHC (a), CD11c (b), B7-1 (c), B7-2 (d), CD40 (e) and ICAM-1 (f). Open histograms indicate the levels of background staining obtained using irrelevant species and isotype-matched control antibodies.

Figure 7: Immunostimulatory activity of LPS-treated esDC. Mature esDC stimulate the strong proliferation of naive, allogeneic T cells (closed circles) but only weak proliferation of syngeneic cells (open triangles). At the same time point, equivalent numbers of immature esDC fail to stimulate either allogeneic or syngeneic cells (open circles and closed triangles respectively).

Figure 8: A comparison of the immunostimulatory activity of myeloid (closed circles) and 'lymphoid' esDC (open circles).

Figure 9: A comparison of the antigen-processing activity of myeloid and lymphoid esDC. At the top dose of DC, the lymphoid population (hatched bar) are considerably less able to present antigen to the hybridoma than myeloid DC (filled bar), although both induce widespread cell death.

Figure 10: Generation of esDC stably transfected with GFP following introduction of the transgene into the parent ES cell line. (a) Colony of ESF116 viewed under fluorescent confocal microscopy showing expression of GFP far in excess of the level of autofluorescence associated with the monolayer of embryonic fibroblasts (b). (c)-(d) Embryoid bodies derived from the ESF116.EGFP clone showing retention of the transgene during differentiation. (e)-(f) Representative esDC developing from transfected embryoid bodies viewed under phase contrast (e) and fluorescence microscopy (f) confirming expression of GFP by terminally-differentiated cells.

3. Delete the text from page 23, line 12 beginning with the phrase "Figure Legends" to page 24, line 32, ending with the phrase "terminally-differentiated cells."

Examiner's Comment

The Amendment, filed 1/13/05, has not been entered. The specification amendment contains redundant information which was filed in the preliminary amendment, filed 5/4/01, and additionally acknowledged in a telephonic interview with Carol Francis on February 2, 2007; accordingly, the amendment will not be entered.

Reasons for Allowance

The following is an examiner's statement of reasons for allowance: the claims are directed to methods of producing either human or mouse dendritic cells, by culturing embryoid bodies made from either human/mouse ES cells in a composition comprising IL-3, and recovering the resultant human/mouse dendritic cells. The closest prior art made of record and not relied upon is Keller *et al.* (Mol. Cell Bio.,

13(10): 473-486 (January 1993) who teach culturing mouse embryoid bodies in the presence of various factors, including IL-3. However, Keller's methods are directed to producing hematopoietic cells, not the instantly claimed dendritic cells; additionally, Keller *et al.* do not anticipate or make obvious the claimed invention, because they do not recover dendritic cells from their culture.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Thaian N. Ton whose telephone number is (571) 272-0736. The Examiner can normally be reached on Monday through Thursday from 7:00 to 5:00 (Eastern Standard Time). Should the Examiner be unavailable, inquiries should be directed to Peter Paras, SPE of Art Unit 1632, at (571) 272-4517. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the Official Fax at (571) 273-8300. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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PATENT EXAMINER